REMARKS

I. Status of the Claims

Claims 246-252, 255, 264, 265, 273, 274 and 276-279 were pending and examined in the October 14, 2011 Office Action. With this Reply, claim 246-250, 252, 264, 265, 273 and 278 are amended and claims 280 and 281 are newly added. Support for the amendments is found at least at para. 118 at p. 8, para. 128 at p. 9, para. 363 at p. 25, and 384-385 at p. 27 of the specification published as US2001/0007767. Claims 246-252, 255, 264, 265, 273, 274 and 276-281 are presented for reconsideration.

II. Rejections under 35 U.S.C. 112, Second Paragraph

A. Claim 273 is rejected under 35 U.S.C., second paragraph, as being unclear. The Office Action states "…it appears from the claim that the third nucleic acid strand comprises a modified nucleotide or analog with said non-nucleic acid entity." In response, Applicants note that claim 273 as amended is clear that the third strand does comprise the modified nucleotide or analog with the non-nucleic acid entity.

The Action also states that claim 273 "…is interpreted such that the polynucleotide tail can be two nucleotides that are complementary to a third strand comprising a non-nucleic acid entity." Applicants disagree, since the polynucleotide tail is hybridized to a portion of the third strand so the polynucleotide tail must be long enough to hybridize to that portion of the third strand. The minimum length of the polynucleotide tail would be understood to vary depending on the sequence of that tail, and that minimum length could be discerned for any sequence by methods known in the art.

In light of the claim amendments and the above discussion, Applicants request withdrawal of this rejection.

B. Claim 278 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for depending from a canceled claim. This rejection is moot since claim 278 as amended does not depend from a canceled claim.

III. Rejections under 35 U.S.C. § 103(a)

A. Claims 246-252, 255, 264, 265, 274 and 276-279 are rejected under 35 U.S.C. 103(a) as being unpatentable over Craig et al. (U.S. 5,766,902) et al., Wagner et al. (U.S. PNAS 1992), and Perales et al. (Eur. J. Biochem., Vol. 226:255-266. The Action continues to assert the points made in the January 20, 2011 Office Action, that

> Craig et al. taught methods for enhancing the targeted delivery of nucleic acid molecules to cells by coupling the nucleic acid to a ligand having affinity for a cell surface molecule or receptor….Specifically recommended are antibodies, growth factors, and fusogenic peptides…. The ligand may be chemically conjugated by covalent bonded to the nucleic acid….
>
> Wagner et al. teach the use of ligand mediated constructs to deliver DNA to cells and state that delivery from endosomes is a limiting step that can be solved by the additional use of a fusogenic peptide….
>
> Perales et al. discuss the concept of ligand mediated delivery of DNA and outlines the design elements that are useful. Perales et al. teach the DNA ligand needs to be efficiently transported to the nucleus and this active process that requires the use of nuclear localization elements….

January 20, 2011 Office Action at pp. 7-8. Applicants respectfully request reconsideration and withdrawal of this rejection in light of the claim amendments and the following discussion.

The claims as amended recite that "said fusogenic peptide and/or the ligand to a cell receptor is on a different nucleic acid strand as the template". None of the cited references, alone or in combination, teach or suggest that any targeting component in a construct is present on a different nucleic acid strand as a template. Such a

configuration is advantageous and non-obvious over a construct having a fusogenic peptide on the same strand for the reasons discussed at least at para. 110 on p. 7 of US2001/0007767. See also para. 22-26 at p. 3 of US2001/0007767, describing problems solved by such a configuration.

Since the cited references, alone or in combination, do not teach or suggest that a fusogenic peptide and/or a ligand to a cell receptor could or should be on a different nucleic acid strand as the template, those references do not render the instant claims obvious. Withdrawal of the rejection under 35 U.S.C. 103(a) is thus respectfully requested.

B. Claim 273 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meyers et al. (EP 0 273 085). The Office Action asserts that Meyers et al. teach a construct that "…comprises double stranded DNA conjugated to at least one molecule of … EGF…[that] is shown to facilitate entry of the nucleic acid into the cell…. [The EGF is coupled] to a 5'-phosphate, thereby producing a modified nucleotide…..[Since] there are only two 5'-phosphates in a linear dsDNA molecule, it is reasonable to presume that the method used by Myers to produce the EGF-dsDNA conjugate results in some dsDNA molecules having one EGF molecule in solely one strand of the dsDNA….[and] one of skill in the art would reasonably have predicted that the constructs disclosed by Myers would have the same properties and would function in substantially the same manner regardless of whether the constructs contained one or two molecules of EGF…." Applicants respectfully request reconsideration and withdrawal of this rejection in light of the claim amendments and the following comments.

Myers et al. do not teach or suggest several aspects of claim 273 as amended. Myers et al. do not teach or suggest a construct having (a) three nucleic acid strands; (b) a cell targeting moiety on a different strand as the template; (c) a second strand having a polynucleotide tail and a region that is complementary and hybridized to the template strand; and (d) a third strand that is complementary and hybridized to a

polynucleotide tail. Further, the construct of Myers et al. would not function "substantially in the same manner" as the claimed construct, for the reasons discussed under **III.A.** above. In particular, the claimed construct has the cell targeting moiety on a different strand as the template thus having the advantages discussed at least at para. 110 on p. 7 of US2001/0007767.

Since Myers et al. do not teach or suggest several aspects of claim 273 and the construct of claim 273 has advantages over any construct taught in Myers et al., that reference does not make claim 273 obvious. Withdrawal of this rejection is therefore respectfully requested.

IV. Double Patenting

Claims 246-252, 255, 264, 265, 271, 273 and 274 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting (OPD) as being unpatentable over claims 245-248, 251, 253, 261-265, 306 and 307 of copending Application No. 08/978,633. Since this rejection is dependent on the scope of both the instant claims and the claims in the cited application, Applicants will provide a terminal disclaimer where necessary when a proper ODP rejection is the only rejection remaining in this application.

V. Conclusion

In view of the foregoing remarks, Applicants respectfully request withdrawal of rejections of record and passage of the claims to allowance.

Applicants authorize the United States Patent and Trademark Office to charge all fees required to maintain pendency of this application, including the extension of time and Request for Continued Examination fees, to Deposit Account No. 05-1135.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney requests that he be contacted at the

number provided below.

Respectfully submitted,

/Elie H. Gendloff/

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